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A Review on Moderate Alcohol Consumption and the Immune System

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ABSTRACT: ***A growing body of research indicates that consuming small quantities of polyphenol-rich alcoholic drinks like wine or beer may be beneficial to one's health. Scientists have long debated the effects of alcohol on immune function, finding that high doses of alcohol can directly suppress a wide range of immune responses on the one hand, and that alcohol abuse is linked to an increased incidence of a variety of infectious diseases on the other. Moderate alcohol consumption, on the other hand, appears to have a protective effect on the immune system when compared to alcohol abuse or abstinence. As a result, the relationship between alcohol consumption, immune response, and infectious and inflammatory processes is still a mystery. With this in mind, it's important to remember that other factors, both directly and indirectly related to immune function, such as drinking habits, beverage type, amount of alcohol consumed, and gender differences, will influence the impact of alcohol consumption on the immune system. This review summarizes published research on the effects of light to moderate amounts of polyphenol-rich beverages such as wine or beer on healthy adults' immunity.***

KEYWORDS: ***Alcohol, Immunity, Polyphenol-Rich, Beverages.***

1. INTRODUCTION

The Seven Countries Study sparked scientific interest in the positive health benefits of moderate alcohol intake in the late 1950s. Numerous epidemiological research since then have shown the negative association between moderate alcohol use and cardiovascular risk morbidity and death. In terms of the immune system, scientists have long debated the impact of alcoholic drinks on host defense. Alcohol may decrease immunological responses directly, and clinical investigations have linked alcohol misuse to an increased prevalence of a variety of viral illnesses. Although acute and chronic alcohol consumption is harmful to one's health and is often regarded as immunosuppressive, it is unclear whether reported alterations in immune function caused by alcohol are clinically significant. Several studies show that alcoholics have a higher rate of infections, although these links are typically ascribed to alcoholism's associated consequences, such as dietary inadequacies, gastrointestinal and hepatic disorders, and socioeconomic level.

Moderate alcohol intake (up to three to four drinks per day) has, on the other hand, been linked to either no risk or a reduced risk of upper respiratory infections. Since moderate alcohol consumption has been shown to have a positive impact on the immune system when compared to alcohol abuse or abstinence, the link between alcohol consumption, immune response, infectious and inflammatory processes has remained a source of debate and is still not fully understood. Other variables unrelated or indirectly linked to immune function, such as drinking pattern, quantity of alcohol, beverage type, or gender differences, are directly involved in the connection between alcohol use and the immune system when examining the research. This review highlights available data on how moderate alcohol intake may influence immune response regulation in healthy individuals, as well as the factors that influence this modulation [1]–[3].

Research paper UGC CARE Listed (Group -I) Journal Volume 11, Iss 11, Nov 2022

A recent research by an increasing number of specialists interested in the immunomodulatory effects of alcohol found that alcohol intake, both acute and chronic, has substantial immune system modulatory effects. In animal and human models of acute, moderate alcohol intake in vivo, alcohol has been shown to reduce host resistance to subsequent bacterial and viral assaults. The results also show that the effects of acute alcohol consumption are very transitory. More study into the therapeutic implications of such a transient immune decrease after acute, moderate alcohol use is required. Failure to develop a sufficient initial immunological response to pathogens in certain types of infections is likely to have a substantial and potentially long-term effect on the immune system. Because of the possibility of increased vulnerability to HIV, mycobacterial infections, and other diseases, the immune system's response to acute alcohol use is particularly important [4]–[6].

In addition, we're learning more about the complex picture of immunosuppression in chronic alcoholics. More study is needed in the advanced chronic alcoholic population to differentiate the immunomodulation produced by chronic alcohol use from that caused by other immunomodulatory illnesses including malnutrition, vitamin deficiency, and liver disease. To create more focused therapy approaches to relieve chronic drinkers' immunosuppression, researchers must first understand the intricacies of immunological alterations caused by chronic alcohol use [7]–[9].

Healthy individuals utilize both innate (non-specific) and acquired (specific) immunity to protect themselves against germs. Innate immunity includes phagocytes like neutrophils and macrophages, natural killer (NK) cells, circulating molecules like complement, and macrophage-derived soluble mediators before exposure to pathogens. When a person is exposed to foreign chemicals (antigens), they develop acquired immunity, which is a complex system of defense in which numerous cells and molecules collaborate. As a result of complex cross-talk between T and B lymphocytes, antigen-presenting cells (monocytes, macrophages, dendritic cells, B lymphocytes), and antigen-presenting cells (monocytes, macrophages, dendritic cells, B lymphocytes), acquired immunity includes humoral and cell-mediated immune responses, as well as specific antibodies and lymphocyte-derived cytokines (monocytes, macrophages, dendritic cells, B lymphocytes). Exogenous chemicals that change any of these immune system components, on the other hand, may jeopardize this well-coordinated anti-infection defense system [10].

Alcohol has been recognized as one of the modulators of host defense. The medical literature has long shown immune dysfunction in long-term alcoholics. Chronic alcoholics are more vulnerable to infections from a variety of pathogens, have a lower immune system, and are more likely to develop cancers, particularly tumors of the head, neck, and upper gastrointestinal tract. While hunger, vitamin deficiency, and acute liver cirrhosis may all play a role in immune system issues in persistent drinkers, alcohol is a strong immune system modulator. According to increasing evidence from human and animal research in vivo as well as in vitro studies, alcohol intake seems to impact the immune system on many levels.

1.1. Alcohol content:

Alcohol may impair immunity via a number of ways. Alcohol seems to impede white blood cell migration to injury and infection sites, as well as cause functional abnormalities in T and B lymphocytes, natural killer cells, and monocytes/macrophages, as well as affect cytokine production. Despite the fact that both cell-mediated and humoral immune responses have been found to be reduced in high-dose alcoholics, research in people and animals indicate that low-doses of ethanol may increase the immunological response. In humans, moderate alcohol

Research paper UGC CARE Listed (Group -I) Journal Volume 11, Iss 11, Nov 2022

consumption was linked to a lower chance of getting the common cold in those exposed to rhinoviruses, indicating that moderate alcohol consumption may improve the immunological response, resulting in a more efficient host defense. This impact may be influenced by the kind of beverage (fermented or distilled), as well as the quantity and duration of ethanol consumption.

In terms of cell-mediated immunity, prolonged alcohol treatment in male rats resulted in a decrease in CD3+, CD4+, and CD8+ cell counts. In humans, however, a rise in absolute CD3+ lymphocyte counts was recently discovered following 30 days of moderate beer intake. The findings indicate that the impact of alcohol on T lymphocyte subsets may vary depending on the quantity drank, despite the fact that the first research was conducted in animals and the second in people.

Signaling proteins generated in response to infection or cell injury are known as cytokines. Damaged cells activate the body's defensive mechanisms, which include the production of cytokines, resulting in a vicious cycle of inflammation, cell death, and scarring. The disturbance of cytokine balance and functions is well recognized to be linked with alcoholic disease. In alcoholic individuals with liver cirrhosis, increased serum tumor necrosis factor (TNF) and interleukin (IL)-6 concentrations, as well as reduced IL-10, interferon (IFN), and IL-2 levels, have been observed often. In humans, increased production of IL-2, IL-4, IL-10, and IFN- was discovered after a 30-day intervention of moderate beer intake. In a similar vein, an in vitro research suggests that some of the health benefits of moderate beer consumption may be linked to its capacity to disrupt pro-inflammatory cytokine cascades. Furthermore, moderate alcohol intake (2 ml vodka/kg body weight) has been shown to have multiple anti-inflammatory benefits, including an increase in IL-10 and a reduction in monocyte inflammatory responses, according to researchers.

These findings suggest that moderate alcohol consumption may have a role in the prevention of cardiovascular disease (CVD) through an anti-inflammatory mechanism. This finding emphasizes the significance of considering the quantity of alcohol consumed when assessing the immunological response. As a result, further research focusing on drinking patterns is needed to fully understand the impact of moderate alcohol intake on the immunological response.

1.2. Type of beverage

When researching the health benefits of beer or wine, additional components such as polyphenols, antioxidants, and vitamins are essential to consider26, 27. Due to the production of free radicals during clearance, ethanol may be harmful to immune cells; however, alcoholic drinks containing antioxidants should protect immune cells27, 28. Clarification of how various kinds of alcoholic and non-alcoholic drinks affect distinct biological markers is one of the major issues that need more study, in order to distinguish which effects are attributable to the alcohol per se and which may be linked to other components. The intake of ethanol only resulted in reduced numbers of white blood cells in animal models; however, the same quantity of alcohol ingested as red wine had no effect on the immunological response.

This may be related to the effect of specific chemicals in red wine, which may help to protect the immune system from being suppressed by alcohol27. Similarly, wine consumption, particularly red wine, has been linked to a reduction in the risk of catching a cold29. Nonetheless, this is a contentious issue. Daily moderate alcohol intake (500 mL of a 12% ethanol dilution) and 500 mL of red wine, red grape juice, and dealcoholized red wine at levels

Research paper UGC CARE Listed (Group -I) Journal Volume 11, Iss 11, Nov 2022

inversely related to CVD risk for two weeks had no impact on human immune cell functions30. However, the study's design may be called into question since the length was inadequate to impact the immune system; it would most likely require up to six weeks to observe changes and variations in the immune system.

Moderate consumption of either wine or beer appeared to be associated with lower levels of systemic inflammatory markers in three different European areas in the MONICA study, an epidemiological study (Germany, Scotland, and France). Despite the authors' suggestion that ethanol may be primarily responsible for these drinks' possible anti-inflammatory benefits, this remains debatable owing to the significant concentration of polyphenols and antioxidant vitamins in these fermented alcoholic beverages. In comparison to gin, moderate red wine consumption resulted in a more pronounced reduction in TNF-induced monocyte adhesion to endothelial cells. Furthermore, following 28 days of red wine consumption, Estruch and colleagues discovered an additional anti-inflammatory impact by reducing C-reactive protein (CRP), as well as monocyte and endothelial adhesion molecules, as compared to gin with the same level of ethanol (30 g per day).

Apart from alcohol and polyphenols (quercetin, rutin, catechin, epicatechin, and resveratrol) in red wine, other relevant components (for example, in beer) that could influence the immune system include total carbohydrate and soluble fiber content, minerals, trace elements, and vitamins such as phosphorous, silicon, magnesium, potassium, niacin, riboflavin, piridoxine, and thiamine.

1.3. Disparities between males and females

Women, in general, seem to be more vulnerable to autoimmune or inflammatory disorders, despite having a lower infection risk than males, particularly during premenopausal years. This is due to women's high estrogen levels, which aid in the stimulation of immunity and the battle against illness. Estrogens may regulate immunological response by regulating cytokine expression and lowering pro-inflammatory cytokines, for example. Several studies have looked specifically at gender variations in the effects of alcohol on inflammatory and immunological responses, finding that women are more sensitive to alcohol than men. Women may be more vulnerable to the effects of ethanol because of their combined pharmacokinetic characteristics.

Gender variations in the physiological processing and metabolic clearance of alcohol, as well as differences in nervous system sensitivity to alcohol, may be the processes behind these disparities. According to other studies, the discrepancies are mostly attributable to women's lower alcohol-dehydrogenase activity, rather than variations in stomach emptying or ethanol oxidation in the liver. In addition, research suggests that hormones have a direct role in the gender variations in alcohol intake. It's been claimed that heavy drinking lowers estrogen levels, nullifying estrogen's immune-boosting benefits and reducing a woman's capacity to fight infections and disease. Plasma testosterone levels may also protect the liver from ethanol-induced oxidative stress, according to Colantoni and colleagues. Women had more leukocytes, neutrophils, lymphocytes, and CD3+ cells than males after a month of moderate beer intake. A deeper knowledge of the molecular processes that underpin gender variations in ethanol intake is obviously required.

2. DISCUSSION

Recent study by a growing number of experts interested in the immunomodulatory effects of alcohol has shown that both acute and chronic alcohol consumption have significant immune system modulatory effects. Alcohol has been demonstrated to weaken host resistance against

Research paper UGC CARE Listed (Group -I) Journal Volume 11, Iss 11, Nov 2022

future bacterial and viral assaults in animal and human models of acute, moderate alcohol consumption in vivo. The findings also indicate that the consequences of acute alcohol intake are very temporary. Further research into the clinical consequences of such a transitory immunological decline after acute, moderate alcohol use is needed. In some kinds of infections, failure to mount an adequate first immunological response to pathogens is likely to have a significant and possibly long-term impact on the immune system. The immune system's response to acute alcohol use is of special relevance because of the possibility of increased vulnerability to HIV, mycobacterial infections, and other diseases.

We are also learning more about the complicated picture of immunosuppression in chronic drinkers. In the advanced chronic alcoholic population, further research is required to distinguish the immunomodulation caused by chronic alcohol use from that caused by other immunomodulatory diseases such as malnutrition, vitamin shortages, and liver disease. Understanding the details of immunological changes induced by chronic alcohol use will be required for developing more targeted treatment methods to alleviate chronic drinkers' immunosuppression.

Innate (non-specific) and acquired (specific) immunity are two systems that healthy people use to defend themselves against microorganisms. Prior to exposure to microorganisms, phagocytes such as neutrophils and macrophages, natural killer (NK) cells, circulating chemicals such as complement, and macrophage-derived soluble mediators are all examples of innate immunity. Exposure to foreign substances (antigens) triggers acquired immunity, which includes an integrated system of host defense in which many cells and molecules work together. Acquired immunity includes humoral and cell-mediated immune responses, as well as specific antibodies and lymphocyte-derived cytokines, as a result of complex cross-talk between T and B lymphocytes, antigen-presenting cells (monocytes, macrophages, dendritic cells, B lymphocytes), and antigen-presenting cells (monocytes, macrophages, dendritic cells, B lymphocytes). Exogenous substances that alter any of these immune system components, however, may compromise this well-coordinated defensive mechanism against infections.

One of the modulators of host defense has been identified as alcohol. Immune impairment in persistent alcohol users has long been documented in medical literature. Chronic alcoholics are more susceptible to infections from a range of pathogens, have a worse capacity to fight infections, and are more likely to acquire malignancies, especially cancers of the head, neck, and upper gastrointestinal tract. While starvation, vitamin insufficiency, and severe liver cirrhosis may all contribute to immunological problems in chronic drinkers, alcohol is a powerful immune system modulator. Alcohol consumption seems to affect the immune system at different levels, according to growing data from human and animal research in vivo as well as in vitro investigations.

Aside from the immunomodulatory effects of chronic alcohol use, new research suggests that acute, moderate alcohol consumption may also regulate the immune system. Acute and chronic alcohol consumption may have an impact on the immune system's innate and acquired immunological responses. After acute or chronic alcohol consumption, altered inflammatory neutrophil, leukocyte, and macrophage activities lead to a weakened host defense against microbial infections. Furthermore, alcohol abuse may harm both the humoral and cellular components of a person's immune system. Inadequate immunological defense is caused by impaired B lymphocyte activities and elevated amounts of some kinds of immunoglobulins at the cost of others. Furthermore, impaired cellular immunological responses play a key role in increasing susceptibility to infections after acute or chronic alcohol use.

Research paper UGC CARE Listed (Group -I) Journal Volume 11, Iss 11, Nov 2022

The production of active oxygen radicals, which are results of the oxidative burst, is a critical component in microbial death. Thus, following alcohol exposure, increased generation of oxygen radicals such as superoxide anion and hydrogen peroxide may be a mechanism weakening antibacterial immune response. The generation of superoxide anion and hydrogen peroxide was reduced in alveolar macrophages from rats given ethanol either abruptly or continuously. Inducible nitric oxide synthase, the enzyme responsible for the production of nitric oxide in alveolar macrophages and neutrophils in response to bacterial stimulation, may be inhibited by ethanol.

In a recent research in rats, both acute and chronic alcohol administration reduced alveolar macrophage nitric oxide production, indicating that decreased reactive oxygen radical formation by ethanol-exposed macrophages may contribute to poor antimicrobial defense. Overproduction of reactive oxygen radicals, on the other hand, has been suggested as a possible pathway for alcohol-induced liver injury. Infusing rats with ethanol for 1, 3, or 5 hours increased not only the hepatic output of superoxide anions, but also inducible superoxide generation. Kuepfer cells, not endothelial cells or hepatocytes, were shown to be the biological source of this ethanol-induced superoxide anion. These findings suggest that ethanol's negative impact on reactive oxygen radical generation may result in twofold harm to the host. To begin with, ethanol may prevent the production of reactive oxygen radicals and nitric oxide in alveolar macrophages, where these mediators are critical for microbial death. Second, ethanol seems to enhance the formation of reactive oxygen radicals in the liver, which may mediate or contribute to direct tissue damage.

3. CONCLUSIONS

There is ample data to indicate that polyphenolic-rich alcoholic drinks like wine and beer include chemicals that prevent immune system suppression or may even have a protective impact. In other words, healthy people who drink a low to moderate quantity of beer or red wine on a daily basis may be less prone to infections, and an anti-inflammatory impact may be one explanation for moderate consumption's CVD-protective benefits. However, several problems remain unsolved, necessitating additional investigation. The impacts on the immune system may be attributed to the antioxidants and other ingredients in these kinds of drinks, as well as the tiny quantity of alcohol. Intervention studies may aid in deciphering the mechanisms through which moderate alcohol intake has immunomodulatory effects. However, since interventional endpoint studies in humans are not practical due to ethical issues, long-term dose-response studies are also needed to evaluate the dose-response connection. Finally, although moderate beer or wine intake seems to improve immunological response in healthy people, increasing alcohol use is not advised due to the significant health hazards associated with more than two drinks per day. It's also worth noting that messages on the advantages of moderate alcohol use have always been targeted at adults. All alcoholic beverages should be avoided by children, teenagers, pregnant women, and the elderly.

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